REMARKS

Claims 12-16 and 25-34 are under consideration in the application. Claim 12 has been canceled without prejudice. Claims 16, 25, 26, 29 and 32 have been amended. New claim 35 has been added. Accordingly, Claims 13-16 and 25-35 are currently under consideration.

Support for the amendments may be found throughout the specification and claims as originally filed. Specifically, support for recitation of "95% identical" can be found at least at page 5, lines 8-17.

New claim 35 is drawn to an isolated polypeptide comprising amino acids ***19-227 of SEQ ID NO: 4***. Support for new claim 35 can be found in the instant specification as originally filed at least at page 17, lines 6-8, where the specification discloses that "the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1 or 3, for example....a ***fragment encoding a biologically active portion of a B7-4 protein***." Further, at page 30, lines 22-23, the specification teaches that "[t]ypically, biologically active portions comprise a domain or motif with at least one activity of the B7-4 protein." The specification further discloses at page 30, lines 14-18, that "the extracellular domain of a B7-4 polypeptide comprises the mature form of a B7-4 polypeptide, *e.g.*, ***the IgV and IgC domains***, but not the transmembrane and cytoplasmic domains of a B7-4 polypeptide." Moreover, the specification further discloses at page 29-30, bridging paragraph, that:

> [T]he invention provides ***isolated portions of a B7-4 protein. B7-4 proteins comprise*** a ***signal sequence***, and an ***IgV domain*** and an ***IgC domain***. The signal sequence of SEQ ID NO:2 is shown from amino acids 1-18. The signal sequence of SEQ ID NO:4 is shown from about amino acids 1-18. The IgV domain of SEQ ID NO:2 is shown from about amino acids 19-134 and the ***IgV domain of SEQ ID NO:4 is shown from about amino acids 19-134***. The IgC domain of SEQ ID NO:2 is shown from about amino acids 135-227 and the ***IgC domain of SEQ ID NO:4 is shown from about amino acids 135-227***. The hydrophilic tail of the B7-4 exemplified in SEQ ID NO:2 comprises a hydrophilic tail shown from about amino acid 228-245. The B7-4 polypeptide exemplified in SEQ ID NO:4 comprises a transmembrane domain shown from about amino acids 239-259 of SEQ ID NO:4 and a cytoplasmic domain shown from about amino acids 260-290 of SEQ ID NO:4.

Still further, Figure 4 of the instant application depicts amino acid sequences corresponding to the signal sequence, the IgV domain and the IgC domain of SEQ ID NO:4, indicating that the IgV domain begins with amino acids "FTVTV..." (F corresponds to ***amino acid position 19 of***

SEQ ID NO:4) and terminates with amino acids "...KVNAPY" (Y corresponds to amino acid position 134 of SEQ ID NO:4), and that the IgC domain begins with amino acids "NKINQR..." (N corresponds to amino acid position 135 of SEQ ID NO:4) and terminates with amino acids "...AELVIP" (P corresponds to ***amino acid position 227 of SEQ ID NO:4***). Thus, an isolated portion of B7-4 including the IgV and IgC domains is clearly described in the specification as comprising amino acids 19-227 of SEQ ID NO: 4.

Moreover, the subject matter of claim 35, *i.e.*, amino acid residues 19-227 of SEQ ID NO: 4, is encompassed by the subject matter of original claims 13 and 16. Thus, claim 35 does not require further searching. Finally, Applicants wish to point out that corresponding claims drawn to a nucleotide sequence encoding amino acids 19-227 of SEQ ID NO:4 have been allowed in the parent application, U.S. Serial No. 09/644,934 (see claims 78-83 of the application).

No new matter has been added by way of these amendments to the specification and claims. Cancellation of and/or amendments to the claims should in no way be construed as acquiescence to any of the Examiner's rejections and were done solely to expedite prosecution and to reduce the number of issues on Appeal. Applicants reserve the option to further prosecute the same or similar claims in the instant or in another patent application(s).

Acknowledgement of the Examiner's Withdrawal of Certain Previously Presented Rejections

Applicants gratefully acknowledge the Examiner's withdrawal of the previous objections to the specification as set forth in the previous Office Action dated June 29, 2004. Further, Applicants gratefully acknowledge the Examiner's withdrawal of the following claim rejections: (a) The previous rejection of claims 12-16 under 35 U.S.C. §112, second paragraph for indefiniteness; (b) The previous rejection of claims 13-16 under 35 U.S.C. §112, second paragraph for lack of written description; (c) The previous rejection of claims 13-16 under U.S.C. §112, first paragraph for lack of enablement; and (d) The previous rejection of claim 12 under 35 U.S.C. §102(b).

Acknowledgement of the Examiner's Indication of Allowability

Applicants gratefully acknowledge the Examiner's indication that claims 13-15 are allowable.

Rejection of Claims 16 and 25 Under 35 U.S.C. §112, Second Paragraph

Claims 16 and 25 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite based on the recitation of "from about amino acids 19-245 of SEQ ID NO: 2 or from about amino acids 19-238 of SEQ ID NO: 4" because... "it is unclear whether the recitation refers to a fragment of e.g. SEQ ID NO: 2 of 19 to 238 amino acids in length, or to a fragment of SEQ ID NO: 2 from amino acid 19 to amino acid 238."

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 16 and 25 have been amended to recite "***from about amino acid residue 19 to amino acid residue 245*** of SEQ ID NO:2 or ***from about amino acid residue 19 to amino acid residue 238*** of SEQ ID NO: 4." This rejection is thereby rendered moot.

Claim 25 is further rejected as being indefinite based on the recitation of "polypeptide consisting of from about amino acids" and states that "the combination of closed language in the recitation of 'consisting' with the open language of 'about' cr[e]ates an ambiguity, so that one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention."

Applicants respectfully traverse the rejection. However, to expedite prosecution, claim 25 has been amended to remove the open term "about." Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection of Claims 12 and 26-34 Under 35 U.S.C. §112, First Paragraph
Written Description

Claims 12 and 26-34 are rejected under 35 U.S.C. §112, first paragraph, as not meeting the Written Description Requirement. Applicants note that claim 12 has been canceled without prejudice. Therefore, this rejection is moot as it pertains to claim 12.

Claims 26-28

The Examiner states that:

> the hybridization conditions recited in the claim (e.g. washing at 50°C) are only moderately stringent, and therefore allow a high degree of sequence variation...in the absence of a recitation that requires hybridization to occur over the full length of the respective molecules, the claim language encompasses fragments of the sequence... [a]pplicant has not provided adequate written description of structural

> features common to fragments of SEQ ID NO: 2 or 4... such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim.

Applicants respectfully traverse this rejection. However, to expedite prosecution, claim 26 has been amended to specify that the nucleic acid molecule "hybridizes ***over its full-length***" and to specify that the hybridization conditions include "washing in 0.2 X SSC, 0.1% SDS, at ***50-65°C***." In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 29-34

With respect to claims 29 and 32, and claims 30-31 and 33-34 which depend from claim 29 and 32, respectively, the Examiner states that "the recitation of 90% identity language is not seen as providing adequate written description of structural features common to the claimed sequences, nor is it seen as defining or limiting the structure of any such sequences such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim."

Applicants respectfully traverse. Applicants would like to bring to the Examiner's attention Example 14 of the *Revised Interim Written Description Guidelines Training Materials*. This example provides that a claim directed to variants of a protein having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" with an accompanying specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. §112, first paragraph for written description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that ***"[t]he single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity***." The Guidelines also provide that "[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art."

As amended, claims 29-34 are directed to polypeptides encoded by nucleic acid molecules that are at least 95% identical to SEQ ID NO:1 or 3, or polypeptides that are at least 95% identical to SEQ ID NO:2 or 4, wherein the polypeptide costimulates T cell proliferation *in vitro* when the polypeptide is present on a first surface and a molecule that transmits an activating signal via the T cell receptor is present on a second, different surface. As set forth in Example 14 of the Written Description Guidelines, the production of polypeptides which contain a 5% variation from a specific sequence is routine in the art. Furthermore, Applicants have disclosed in the instant specification assays for identifying all of the at least 95% identical polypeptides of SEQ ID NO:2 or 4 that are capable of costimulating T cell proliferation *in vitro*, *i.e.*, a costimulation assay in which the polypeptide is present on a first surface and a molecule that transmits an activating signal via the T cell receptor is present on a second, different surface (see, for example, Example 4 at page 99 of the specification). Thus based on the teachings in Applicants' specification, the ordinary skilled artisan would conclude that Applicants were in possession of the claimed invention at the time of filing the instant application.

Moreover, Applicants respectfully draw the Examiner's attention to the claims drawn to the corresponding nucleic acids which have been allowed in the parent application, U.S. Serial No. 09/644,934. Such claims were deemed to satisfy the Written Description requirement and, therefore, patentable by the U.S. Patent Office and are substantively identical to pending claims 29-34 of the instant application.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Rejection of Claims 12-16 Under 35 U.S.C. §112, First Paragraph - Enablement

Claims 12-16 are rejected under 35 U.S.C. §112, first paragraph, "because the specification, while being enabling for isolated polypeptides of SEQ ID NO:2 or 4, or encoded by nucleic acids of SEQ ID NO:1 or 3, does not reasonably provide enablement for the various polypeptides comprising fragments of, or encoded by nucleic acids which hybridize to, or are at least about 90% identical to the recited sequences... [t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." Claim 12 has been canceled without prejudice. Therefore, this rejection is moot as it pertains to claim 12.

Claims 26-28

The Examiner rejects claims 26, and claims 27-28 which depend therefrom, and states that "the hybridization language [recited in the claim]....first, as noted supra, ... reads on fragments, and second, requiring only moderate stringency ... allows for an extremely large number of variant sequences."

While in no way acquiescing to the validity of the rejection, and solely to expedite prosecution, claim 26 has been amended to specify that the nucleic acid molecule "hybridizes ***over its full-length***" and to specify more stringent hybridization conditions of "washing in 0.2 X SSC, 0.1% SDS, at ***50-65°C***." Applicants therefore respectfully request that the Examiner reconsider and withdraw this rejection.

Claim 29-34

The Examiner states that "the 90% identity language allows for an extensive sequence variation, such that it is unpredictable, without undue experimentation, which of the numerous possible variants posses the functional properties of B7-4 molecules."

Applicants traverse this rejection. Claims 29-34 as currently amended are directed to polypeptides encoded by nucleic acid molecules that are at least ***95% identical*** to SEQ ID NO:1 or 3, or polypeptides that are at least ***95% identical*** to SEQ ID NO:2 or 4, and ***wherein the polypeptide costimulates T cell proliferation in vitro*** when the polypeptide is present on a first surface and a molecule that transmits an activating signal via the T cell receptor is present on a second, different surface. Based on Applicants' teachings in the present specification, combined with the knowledge and level of skill in the art, the claimed invention is fully enabled.

The factors to be considered when determining whether the claimed subject matter is enabled (*i.e.*, whether undue experimentation would be required to make or use the claimed invention) include, *inter alia*, the amount of direction or guidance presented in the specification, the state of the prior art and the relative skill of those in the art and the predictability in the art. *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). The test of enablement is not whether any experimentation is necessary, but whether if any required experimentation is undue. *In Re Angstadt,* 537 F.2d 498, 190 USPQ 214 (CCPA 1976); M.P.E.P. §2164.01.

In the instant application, detailed guidance is provided in the specification regarding how to produce the claimed polypeptides encoded by nucleic acid molecules that are at least

95% identical to SEQ ID NO:1 or 3 and the claimed polypeptides which are at least ***95% identical*** to the amino acid sequence of SEQ ID NO:2 or 4 (see, for example, page 34, line 6 to page 36, line 4 and page 29, line 25 to page 31, line 6). Further, Applicants have disclosed in the instant specification assays for identifying all of the at least 95% identical polypeptides of SEQ ID NO:2 or 4 that are capable of costimulating T cell proliferation *in vitro*, *i.e.*, by using a costimulation assay in which "the polypeptide is present on a first surface and a molecule that transmits an activating signal via the T cell receptor is present on a second, different surface" (see, for example, Example 4 at page 99 of the specification).

Furthermore, at the time of the present invention it was well-known how to produce polypeptides which contain a 5% variation from a specific sequence. Indeed, Applicants again respectfully draw the Examiner's attention to Example 14 of the *Revised Interim Written Description Guidelines Training Materials*. As discussed above, the Guidelines provide in Example 14 that "***[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art*** and ***an assay is described which will identify other proteins having the claimed catalytic activity.*** Moreover, ***procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.***" Thus, as set forth in Example 14 of the Written Description Guidelines, the production of polypeptides which contain a 5% variation from a specific sequence is routine in the art.

Still further, as stated above, Applicants have disclosed an assay for identifying all of the at least 95% identical polypeptides of SEQ ID NO:2 or 4 that are capable of costimulating T cell proliferation *in vitro*. T cell costimulation assays such as that disclosed in the instant specification were well known at the time of the present invention. Employment of the T cell costimulation assay to identify polypeptides which retain the ability to costimulate T cell proliferation would be nothing more than routine to those skilled in the art.

Thus, it is clear that, once provided with the amino acid sequence or nucleic acid sequence encoding a given polypeptide, there was a high level of skill in the art at the time of the invention with respect to generating variants which retain the ability to costimulate T cell proliferation *in vitro*. Thus, one of ordinary skill in the art would have been able to have made and identified all of the at least 95% identical polypeptides of SEQ ID NO:2 or 4 which retain the ability to costimulate T cell proliferation without undue experimentation.

Finally, Applicants respectfully draw the Examiner's attention to the claims drawn to the corresponding nucleic acids which have been allowed in the parent application, U.S. Serial No.

09/644,934. Such claims were deemed to satisfy the Enablement requirement and, therefore, patentable by the U.S. Patent Office and are substantively identical to pending claims 29-34 of the instant application.

In view of the foregoing, Applicants respectfully submit that an ordinarily skilled artisan reading the foregoing teachings in Applicants' specification would have been able to practice the claimed invention using only routine experimentation. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 26-28 Under 35 U.S.C. §112, First Paragraph- Written Description

Claims 26-28 are rejected under 35 U.S.C. §112, first paragraph, as not meeting the Written Description requirement. In particular, the Examiner contends that the instant claims now recite limitations of "50-60°C" which "were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed." The Examiner states that the specification "discloses a different range of 50-65°C."

Applicants respectfully traverse this rejection. The temperature range for the hybridization washing step recited in the claims of "50-60°C" is encompassed by the temperature range of "50-65°C" described in the specification and is, therefore, not new matter. However, to expedite prosecution, claims 26-28 have been amended to recite the range of "50-65°C." In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

SUMMARY

Based on the foregoing, reconsideration and withdrawal of all the rejections is respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution, the Examiner is urged to call the undersigned.

Applicants believe no additional fees to be due at this time. However, if additional fees are due, please charge our Deposit Account No. 12-0080, under Order No. GNN-004ADV from which the undersigned is authorized to draw.

Dated: August 29, 2005

Respectfully submitted,

By _____

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